The Treatment of Juvenile Fibromyalgia with an Intensive Physical and Psychosocial Program

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Objective To assess the short-term and 1-year outcomes of children with fibromyalgia treated with intensive physical and occupational therapy (PT/OT) and psychotherapy.

Study design Children with fibromyalgia seen at a tertiary care hospital were treated with 5-6 hours of intensive PT/OT daily and at least 4 hours of psychosocial services weekly. All medications used for fibromyalgia were discontinued. Children underwent standardized testing, including a visual analog scale for pain; the Bruininks-Oseretsky Test of Motor Performance, Second Edition; the Bruce treadmill protocol; the Functional Disability Inventory; the Pain Stages of Change Questionnaire, adolescent version; and the Pediatric Quality of Life Inventory, Teen Report, at 3 time points: at program entry, at the end of the intensive program, and 1 year after the end of the program.

Results Sixty-four children (median age, 16 years; 95% Caucasian; 94% female; median duration of symptoms, 21 months) were studied. The mean pain score decreased significantly from program entry to the end of the program (from 66 of 100 to 25 of 100; $P = .001$). At the 1-year follow-up, 33% reported no pain. All measures of function on the Bruininks-Oseretsky Test of Motor Performance, Second Edition improved significantly and remained at that level or continued to improve over the subsequent year. The mean Bruce treadmill protocol time first increased from 588 seconds to 801 seconds ($P < .001$) and then dropped to 750 seconds ($P = .005$), which is at the 90th percentile for age and sex. All Pain Stages of Change Questionnaire, adolescent version subset scores improved significantly initially and were stable or improved at 1 year, as did the Pediatric Quality of Life Inventory, Teen Report total score.

Conclusion Children with fibromyalgia can be successfully treated without medications with a very intensive PT/OT and psychotherapy program. They have significantly improved pain and function by subject report and objective measures of function. *(J Pediatr 2015;167:731-7)*.

Fibromyalgia is one of the most common amplified pain syndromes in children, occurring in 2%-6% of the pediatric population.[1-5] It is defined as widespread pain lasting at least 3 months and, depending on criteria, associated with between 5 and 11 of 18 trigger points, along with other somatic complaints, such as irritable bowel syndrome, fatigue, unrestorative sleep, and chronic headache.[6,7] Girls predominate at a rate of approximately 4:1, and the disorder seems to affect Caucasians disproportionately.[8] The etiology is unknown, but some of the factors associated with adults with fibromyalgia include depression,[5,9] low pain threshold,[2] cortisol dysregulation,[10,11] and ischemia.[12-14] Adult fibromyalgia criteria are applied in diagnosing these children, and as such other potential etiologies need to be ruled out before a diagnosis can be made. No criteria have been established for the diagnosis of fibromyalgia in children.

Treatment of childhood fibromyalgia has remained elusive, with the major focus on cognitive behavioral therapy[15-17] and aerobic training.[18,19] Studies of long-term outcomes have reported persistent pain in more than 90% of affected children, and sleep disturbance was found in more than 90% of 33 children with fibromyalgia surveyed 2.6 years after diagnosis.[20,21] In a large cohort of children with fibromyalgia, more than 80% had persistent symptoms into adulthood, and, compared with controls, had more pain, anxiety, and medical visits, along with decreased physical function at 5.9 years after diagnosis.[22] In adults, evidence-based guidelines stress cognitive behavioral therapy and aerobic training.[23] Medications have little role in treating children, and systematic reviews in adults are not encouraging.[24-27]

We have had short- and long-term success in treating children with complex regional pain syndrome with a very intensive physical and occupational therapy (PT/OT) program along with psychological counseling,[28] which has been replicated by others.[29,30] Although complex regional pain syndrome is a different pain diagnosis, children with this form of amplified pain are also treated in our program,

BOT-2	Bruininks-Oseretsky Test of Motor Performance, Second Edition
FDI	Functional Disability Inventory
PedsQL	Pediatric Quality of Life Inventory
PSOCQ-A	Pain Stages of Change Questionnaire, adolescent version
PT/OT	Physical and occupational therapy
VAS	Visual analog scale

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and we have studied them previously. We also have reported short-term functional outcomes in a small group of children with fibromyalgia who underwent sleep studies before and after participating in the intensive PT/OT program with excellent results.[18]

The objective of the present study was to compare a cohort of patients with fibromyalgia on various objective and subjective measures at 3 time points: at admission to our program, discharge from the program, and 1 year after completion of the program.

Methods

The study protocol was reviewed and approved by our hospital's Committee for the Protection of Human Subjects. All parents provided consent, and subjects provided assent before study participation. The source population for the study was children and adolescents aged 13-18 years with a diagnosis of primary juvenile fibromyalgia treated in the inpatient or day hospital amplified musculoskeletal pain program between September 2008 and May 2011. The subjects were a convenience sample enrolled without regard to pain duration, pain severity, or previous therapy. Children for whom this was not the initial participation in the amplified musculoskeletal pain program, as well as those whom required modification of the program because of another medical condition, such as cerebral palsy or fragile bones, were excluded. One patient who consented to participate was discharged from the program before completing any therapy owing to high-level contact precautions (methicillin-resistant *Staphylococcus aureus* carrier). All subjects fulfilled the American College of Rheumatology's 2010 fibromyalgia criteria.[31]

Intervention

Before participating in our program, the children were encouraged to do aerobics and, if they had allodynia, to desensitize. We frequently prescribed a formal home exercise program and local physical therapy, although adherence was not formally measured. All pain medications and medications given for fibromyalgia, such as analgesics, antiepileptics, antidepressants, and sleep medications, were discontinued. If the home exercise program was not successful, then the dose of PT/OT was increased. It is these children who are included in this report.

The children were treated either as day hospital patients or inpatients. All children received individualized 1-on-1 therapy for 5-6 hours a day, with the focus on quickly reestablishing normal function, along with maximizing aerobic conditioning. Activities typically included timed activities (eg, animal walks, stepping in/out of a tub, running up and down stairs, stepping and squatting activity), scooter boards, treadmill, elliptical, stairs, long-distance community ambulation, strengthening and endurance activities, and dance or other video game activities. Treatment goals were set high and quickly advanced as the child progressed through the requirements to a higher level of function and exercise. Children with allodynia received multiple courses of desensitization, including rubbing, local and total body vibration, constant light touch or compression, temperature and noise desensitization, fanning, and exposure to multiple different textures. Desensitization was often incorporated into exercises when possible. Children who experienced pain with eating were often required to eat a minimum of 7 meals and snacks per day.

The duration of therapy for each child was individually determined by the treatment team based on physical functioning goals obtained, rate of improvement, and judgment regarding the child's ability to sustain and further improve on these functional goals in the home environment without formal physical therapy.

Psychosocial support included both 1-on-1 and group sessions with a psychologist for both cognitive and behavioral therapy-based intervention, as well as support for coping during PT/OT sessions, as indicated. Art therapy and music therapy were also included, for a minimum of 4 hours per week of psychosocial support. In addition, parent group sessions were held weekly, and family or parent sessions were added when indicated.

Objective

The objective of this study was to evaluate long-term functional and psychosocial outcomes of the patients completing our intensive program.

Outcome Measures

Bruce Treadmill Protocol[32]: This test consists of walking on a treadmill until the subject is unable to continue walking or running owing to exhaustion or pain. The test increases in speed and incline every 3 minutes until the subject cannot continue or he or she completes the test time of 21 minutes. The patient is allowed to hold the handrail(s) of the treadmill if he or she chooses. The test results can be compared with age- and sex-matched norms.

Bruininks-Oseretsky Test of Motor Performance, Second Edition (BOT-2)[33]: This test measures gross and fine motor function, as well as balance and coordination. It consists of 8 subtests: fine motor control, fine motor integration, manual dexterity, bilateral coordination, balance, running speed and agility, upper limb coordination, and strength. The scores on these subtests are summed to calculate a total composite score, which is then interpreted based on age- and sex-matched norms. For each subtest, higher scores represent better performance.

Functional Disability Inventory (FDI)[34]: This self-report measure asks the subject to rate how much physical "trouble" he or she experiences related to pain when attempting to complete various functional activities. Responses include "no trouble," "a little trouble," "some trouble," "a lot of trouble," and "impossible." These ratings are given a number equivalent. These numbers are summed to arrive at a final score ranging from 0 to 60,

with lower scores indicating higher levels of function and higher scores indicating higher levels of disability due to pain.

Pain Stages of Change Questionnaire, adolescent version (PSOCQ-A)[35]: This tool is based on Prochaska and DiClemente's transtheoretical model of behavior change, which assesses an individual's motivation to change and to engage in treatment. When adapted for use in patients with chronic pain, 4 stages of change are identified: precontemplation (no clear sense of responsibility for pain control or need to make behavioral change), contemplation (some awareness of responsibility for pain control and some need to make behavioral change), action (actively taking responsibility for pain control and making behavioral change), and maintenance (maintaining responsibility for pain control and maintaining behavioral change). The subject responds to each of the 30 items on this measure on a 5-point scale ranging from "strongly disagree" to "strongly agree." This measure is scored by summing the scores of the different item numbers composing each of the 4 stages, and then dividing that total by the number of items in that domain. The higher a subject scores in a specific domain, the more emphasis he or she is placing on that stage of change with regard to readiness to take responsibility for the pain and make behavioral changes.

Visual analog scale (VAS): To use this tool, the subject is asked: "How much pain are you in now?" The subject is given a card on which is printed a 100-mm line and asked to mark his or her level of pain intensity on the scale, with 0 mm being no pain and 100 mm being the worst pain imaginable. This scale has proven validity.[36]

Pediatric Quality of Life Inventory (PedsQL), Teen Report (Mapi Research Trust, Lyon France)[37-40]: This 23 item self-report measure assesses health-related quality of life in patients aged 13-18 years with regard to core health dimensions, including physical functioning, emotional functioning, social functioning, and school functioning. The subject responds to questions assessing how often he or she has problems in these domains on a 5-point scale ranging from "never" to "almost always." Items are reverse-scored and transformed to a scale of 0-100. Mean scores are then calculated for each core health dimension, with lower scores indicating poorer quality of life. Summary scores are also created. The psychosocial health summary score is the sum of the emotional, social, and school functioning scales. The physical health summary score equals the physical functioning scale score. The total score is the sum of all the items answered over all of the scales.

All measures were administered once at each of the 3 study time points.

Statistical Analyses

Demographic information and baseline characteristics are summarized by frequency and percentage for categorical variables (eg, race, pain diagnosis) and by mean and 95% CI or median and IQR, as appropriate, for continuous or count variables (eg, age, duration of pain, duration of the intensive program).

The median function, pain, and quality of life measures recorded at the following time points were compared using a matched signed-rank test: preprogram clinic visit and program entry, program entry and completion, and program completion and 1 year after program completion. For those subjects missing discharge measures (<15% for all measures), sensitivity analyses were performed, which assumed no improvement in scores from program entry to program completion.

Results

Subjects were recruited between 2008 and 2011, with follow up continuing through 2012.

Baseline Data

Sixty-four of the 81 children and adolescents with primary fibromyalgia who participated to The Children's Hospital of Philadelphia's intensive pain program were enrolled (79%). The enrolled subjects and those who were not enrolled did not differ significantly in terms of pain intensity (as measured by the VAS) at program entry. Demographic data, duration of pain, and self-reported comorbid psychiatric diagnoses are presented in Table I. Twenty-three subjects (36%) had a concomitant diagnosis of anxiety (n = 6), depression (n = 8), or both (n = 9). Thirty-seven subjects (58%) were on pain medication other than acetaminophen or a nonsteroidal anti-inflammatory drug at the time of enrollment. All pain medications, including acetaminophen and nonsteroidal anti-inflammatory drugs, were stopped at the time of admission to the program. The mean duration of the inpatient or day hospital program was 23 ± 13 days.

Subjects had to wait a median of 143 days from program assessment to program entry (Table I). During this period, they were encouraged to be active and participate in outpatient PT/OT and counseling. During the interval between program assessment and program entry, the FDI score improved from 26 to 24, a slightly significant change ($P = .03$) (Table II), and the pain score dropped from 71 to 66, a nonsignificant change ($P = .86$) (Table III).

Outcomes and Estimation

Function. Scores for tests of function at program entry, program completion, and 1 year after program completion are shown in Table II. In every test of function, the subjects' performance improved significantly from program entry to program completion ($P < .001$ for all). Bruce scores decreased slightly over 1 year after program completion, but scores at the 1-year follow-up remained significantly better than those at program entry ($P < .001$), and remained at or above the 90th percentile for age- and sex-matched norms, compared with below

Table I. Patient characteristics (n = 64)

Characteristics	Value
Age, y, median (IQR)	16 (15-17)
Caucasian race, n (%)	62 (95)
Female sex, n (%)	60 (94)
Duration of symptoms, mo, median (IQR)	21 (11-36)
Wait for program entry, d, median (IQR)	143 (97-233)
Duration of intensive program, d, mean ± SD	23 ± 13
Comorbid psychiatric conditions, n (%)	
Anxiety	15 (23)
Depression	17 (27)
Comorbid medical conditions, n (%)	
Juvenile arthritis	3 (5)
Diabetes	2 (3)
Migraine/chronic headache	13 (20)
Sickle cell disease	1 (2)
Thyroid dysfunction	1 (2)
Lyme disease	2 (3)
Ehlers-Danlos syndrome	1 (2)
Psoriasis	1 (2)
Chiari malformation	2 (3)
Chronic kidney disease	1 (2)
FDI at program entry, median (IQR)	24 (17-31)
Pain VAS score at program entry, median (IQR)	66 (44-82)

the 25th percentile at admission. All domains of the BOT-2 remained stable at 1 year after program completion, as did FDI scores.

We performed sensitivity analyses for each measure that assumed anyone with missing discharge data (<11% for all program entry and completion measures) did not have any improvement in scores since program entry. Overall, across all tests of function, there was still significant improvement from program entry to program completion ($P < .001$ for all).

Pain, Quality of Life, and Adolescent Clinical Inventory. Scores for pain, quality of life, and the adolescent clinical inventory at program entry, program completion, and 1 year after program completion are shown in Table III. Subject-reported pain as measured on a VAS improved significantly from program entry to program completion and continued to improve (albeit not to a statistically significant degree) to 1 year after program completion. Of the 54 subjects who had a pain VAS recorded at 1 year after program completion, 18 (33%) had a score of 0/100, indicating no pain, and 26 (48%) had a score of 10/100 or less.

The PSOCQ-A scores suggest that over the course of the program, the subjects tended to shift toward taking more active steps to address their pain, and that they tended to remain active in addressing the pain and maintaining gains (Table III). Specifically, the scores indicate a significant decrease in precontemplation between program entry and program completion, along with a nonsignificant decrease between program completion and 1-year follow-up. Contemplation increased significantly between program entry and program completion and remained stable between program completion and follow-up. The PSOCQ-A scores also indicate a statistically significant increase in action between program entry and program completion and also between program completion and 1-year follow-up. Similarly, maintenance scores also increased significantly between program entry and program completion, but showed no significant change between program completion and 1-year follow-up.

Subject-reported quality of life as measured by the PedsQL, Teen Report significantly improved from program entry to program completion (Table III). The total, physical health summary, psychosocial health summary, and school functioning scores continued to improve significantly throughout the year after program completion. Emotional functioning and social functioning remained stable throughout this period.

Discussion

Our children with long-standing fibromyalgia exhibited significant improvement in nearly all of the functional and pain measures that we applied. Function, as measured by the FDI, went from the moderately disabled category to normal[34] and remained normal for the year after program completion. The BOT-2 battery continued to improve significantly over that 1-year period. The Bruce protocol times improved significantly and remained quite high at the 1-year follow-up, demonstrating durability of aerobic endurance. Although there was a dropoff in the mean time at the 1-year follow-up, it remained at the 90th percentile for normal children.[32] It is understandable that at the end of the intensive PT/OT

Table II. Tests of function

Tests	Median (IQR)				*P* value	
	Before program entry	Program entry	Program completion	1-year follow-up	Program entry vs end	Program completion vs 1-year follow-up
Bruce	-	588 (429-661)	801 (739-908)	750 (676-840)	<.001	.005
BOT-2	-					
Fine manual control		31 (16-54)	48 (31-73)	60 (42-89)	<.001	.07
Manual coordination		31 (16-62)	73 (54-92)	86 (54-96)	<.001	.09
Body coordination		21 (8-49)	46 (27-66)	46 (27-66)	<.001	.69
Strength and agility		35 (14-58)	65 (35-79)	66 (50-76)	<.001	.41
Total motor composite		24 (8-46)	54 (35-84)	69 (38-86)	<.001	.05
FDI	26 (20-33)	24 (17-31)	7 (3-20)	5 (2-18)	<.001	.12

Table III. Pain, adolescent clinical inventory, and quality of life

Tests	Median (IQR)				*P* value	
	Before program entry	Program entry	Program completion	1-y follow-up	Entry vs end	End vs 1-y follow-up
Pain VAS	71 (57-78)	66 (44-82)	25 (4-68)	20 (0-66)	<.001	.05
PSOCQ-A	-					
Precontemplation		2.9 (2.4-3.4)	2.3 (2.0-2.9)	2.14 (1.6-2.9)	<.001	.120
Contemplation		3.6 (3.1-3.9)	3.8 (3.3-4.2)	3.5 (3.0-3.9)	.005	.018
Action		3.7 (3.2-4.0)	4.3 (4.0-4.8)	4.0 (3.3-4.3)	<.001	.006
Maintenance		3.6 (3.0-4.0)	4.4 (4.0-4.9)	4.4 (4.0-5.0)	<.001	.73
PedsQL, Teen Report	-					
Total score		48 (38-60)	66 (51-78)	78 (67-92)	<.001	<.001
Physical health summary score		31 (22-47)	63 (44-81)	78 (59-94)	<.001	<.001
Psychosocial health summary score		55 (45-67)	70 (55-78)	80 (67-92)	<.001	.001
Emotional functioning		50 (40-65)	60 (55-85)	75 (55-85)	<.001	.070
Social functioning		70 (50-80)	85 (70-95)	90 (75-100)	<.001	.140
School functioning		50 (30-60)	55 (45-80)	80 (60-95)	.002	<.001

program, these children would have well-above-average endurance, and the fact that it remained at such a high level at 1 year reinforces their reports of high-level function.

The subjective reported level of pain also decreased significantly, with a mean level of 20/100 at 1 year after program completion. One-third of the subjects reported a pain level of 0/100 and another 15% had a pain score between 1/100 and 10/100.

Program duration varied owing to the individualized nature of the program for each subject. We set PT/OT goals for each subject, and the duration of the program depended on the achievement of those goals, which varied from child to child. The wait time for our program was lengthy because of the waiting list to enter the program, as well as the need to obtain insurance approval; however, this provided an opportunity for us to assess the subjects as their own controls. To fully assess for the observed improvement, we looked at pain and FDI scores from the time of clinic assessment to program entry (**Tables II** and **III**), and found no change in pain during this interval. There was a very slight improvement in function (2 points) on the FDI, but this was not clinically meaningful. This demonstrates that the changes observed throughout the program were real observations and not representative of regression to the mean or a natural course of the disorder.

All children were off pain medication during the intensive PT/OT program, and none were on pain medication at the 1-year follow-up. In our experience, medications in this population lead to side effects and are ineffective, while also perpetuating the sick role by suggesting that reliance on medication is necessary for successful treatment. These children are at great risk of overmedication and iatrogenic injury.

Our data are in marked contrast to those from a previous study that used much less PT/OT.[19] This parallels our experience in treating children with complex regional pain syndrome in whom PT/OT was ineffective, but with a much less intensive program. Both the dose of PT/OT and the quality of the therapy differed from traditional PT/OT, in that we focused on desensitization and prolonged aerobics, strengthening, and functional activities individualized to the subjects, and did not inquire about pain or let pain or the fear of pain stop them. We believe that this focus on function rather than pain helps children break the pain cycle and overcome the long-standing functional and pain limitations with which they presented.

An important aspect of our program is the emotional support of the child and family. Dealing with pain and the often-long process of seeking diagnosis and appropriate treatment is an arduous process, both physically and emotionally, for children and their families. Psychotherapy focuses on using cognitive behavioral therapy-based interventions to support children through intensive PT/OT, as well as helping them apply these strategies to coping with stress in life outside of program demands that may be contributing to their pain. Many children benefit from cotreatment during PT/OT to help learn and use strategies in vivo. Group psychotherapy sessions are also used, along with creative arts therapies to help advance socioemotional goals. Psychotherapy recommendations after the intensive program have included individual, family, marital, and other therapy as indicated. The psychological well being of our sample was significantly improved at the end of 1 year, as demonstrated by the overall improved quality of life and maintenance of a high level of emotional and social functioning. Our finding of lower school functioning at program completion than at the 1-year follow-up is consistent with our program structure, which recommends that patients do not engage in schoolwork during intensive program treatment; however, school functioning improves over the year postdischarge, likely as children catch up on missed work, and remains at a higher level owing to increased function and decreased pain, as well as improvements in overall coping skills.

The philosophy of our program is that the children treat their own pain while learning the tools for doing so in our treatment program. It is our hope that because of this, they will remain fully functional and free of pain in the long term. No studies of this have been conducted to date, however. That said, the psychological variables at play may

better predict long-term outcomes, and addressing these head on may reap greater rewards, especially for long-term outcomes.[5]

A weakness of this study is that it was not a randomized or controlled trial. Nonetheless, these children had long-standing pain that did not remit with less-intensive therapy. Others have reported cohorts of children with fibromyalgia who exhibit minimal improvement up to 6 years postdiagnosis.[20-22] The children in the present study were significantly disabled and were able to achieve and maintain normal function by both self-report and objective measures over 1 year. We speculate that most of these children will have the necessary mental and physical capability to stay well, and if relapses occur, will have the tools to self-reinstitute these measures and resolve any new symptoms, as we have seen in children with complex regional pain syndrome treated with such a program.[28,29]

Children with fibromyalgia can be treated successfully without the use of medications and can regain normal function, achieve remission or marked reduction of pain, and experience increased quality of life with an interdisciplinary approach that uses much more intensive PT/OT than is common in most pain programs, along with cognitive, behavioral, and other psychosocial supports. ■

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References

1. Alayli G, Durmus D, Ozkaya O, Sen HE, Genc G, Kuru O. Frequency of juvenile fibromyalgia syndrome in children with familial Mediterranean fever: effects on depression and quality of life. Clin Exp Rheumatol 2011; 29:S127-32.
2. Buskila D, Press J, Gedalia A, Klein M, Neumann L, Boehm R, et al. Assessment of nonarticular tenderness and prevalence of fibromyalgia in children. J Rheumatol 1993;20:368-70.
3. Clark P, Burgos-Vargas R, Medina-Palma C, Lavielle P, Marina FF. Prevalence of fibromyalgia in children: a clinical study of Mexican children. J Rheumatol 1998;25:2009-14.
4. Durmaz Y, Alayli G, Canbaz S, Zahiroglu Y, Bilgici A, Ilhanli I, et al. Prevalence of juvenile fibromyalgia syndrome in an urban population of Turkish adolescents: impact on depressive symptoms, quality of life and school performance. Chin Med J (Engl) 2013;126: 3705-11.
5. Mikkelsson M, El-Metwally A, Kautiainen H, Auvinen A, Macfarlane GJ, Salminen JJ, et al. Onset, prognosis and risk factors for widespread pain in schoolchildren: a prospective 4-year follow-up study. Pain 2008;138: 681-7.
6. Yunus MB, Masi AT. Juvenile primary fibromyalgia syndrome: a clinical study of thirty-three patients and matched normal controls. Arthritis Rheum 1985;28:138-45.
7. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia: report of the Multicenter Criteria Committee. Arthritis Rheum 1990;33:160-72.
8. Eraso RM, Bradford NJ, Fontenot CN, Espinoza LR, Gedalia A. Fibromyalgia syndrome in young children: onset at age 10 years and younger. Clin Exp Rheumatol 2007;25:639-44.
9. Mikkelsson M, Salminen JJ, Kautiainen H. Non-specific musculoskeletal pain in preadolescents: prevalence and 1-year persistence. Pain 1997;73: 29-35.
10. Macedo JA, Hesse J, Turner JD, Meyer J, Hellhammer DH, Muller CP. Glucocorticoid sensitivity in fibromyalgia patients: decreased expression of corticosteroid receptors and glucocorticoid-induced leucine zipper. Psychoneuroendocrinology 2008;33:799-809.
11. Nicolson NA, Davis MC, Kruszewski D, Zautra AJ. Childhood maltreatment and diurnal cortisol patterns in women with chronic pain. Psychosom Med 2010;72:471-80.
12. Elvin A, Siosteen AK, Nilsson A, Kosek E. Decreased muscle blood flow in fibromyalgia patients during standardised muscle exercise: a contrast media-enhanced colour Doppler study. Eur J Pain 2006; 10:137-44.
13. Klaver-Krol EG, Zwarts MJ, Ten Klooster PM, Rasker JJ. Abnormal muscle membrane function in fibromyalgia patients and its relationship to the number of tender points. Clin Exp Rheumatol 2012;30:44-50.
14. Srikuea R, Symons TB, Long DE, Lee JD, Shang Y, Chomentowski PJ, et al. Association of fibromyalgia with altered skeletal muscle characteristics which may contribute to postexertional fatigue in postmenopausal women. Arthritis Rheum 2013;65:519-28.
15. Degotardi PJ, Klass ES, Rosenberg BS, Fox DG, Gallelli KA, Gottlieb BS. Development and evaluation of a cognitive-behavioral intervention for juvenile fibromyalgia. J Pediatr Psychol 2006;31:714-23.
16. Kashikar-Zuck S, Flowers SR, Strotman D, Sil S, Ting TV, Schikler KN. Physical activity monitoring in adolescents with juvenile fibromyalgia: findings from a clinical trial of cognitive-behavioral therapy. Arthritis Care Res 2013;65:398-405.
17. Kashikar-Zuck S, Ting TV, Arnold LM, Bean J, Powers SW, Graham TB, et al. Cognitive behavioral therapy for the treatment of juvenile fibromyalgia: a multisite, single-blind, randomized, controlled clinical trial. Arthritis Rheum 2012;64:297-305.
18. Olsen MN, Sherry DD, Boyne K, McCue R, Gallagher PR, Brooks LJ. Relationship between sleep and pain in adolescents with juvenile primary fibromyalgia syndrome. Sleep 2013;36:509-16.
19. Stephens S, Feldman BM, Bradley N, Schneiderman J, Wright V, Singh-Grewal D, et al. Feasibility and effectiveness of an aerobic exercise program in children with fibromyalgia: results of a randomized controlled pilot trial. Arthritis Rheum 2008;59:1399-406.
20. Rabinovich C, Schanberg L, Stein L, Kredich DW. A follow-up study of pediatric fibromyalgia patients. Arthritis Rheum 1990;33:S146.
21. Siegel DM, Janeway D, Baum J. Fibromyalgia syndrome in children and adolescents: clinical features at presentation and status at follow-up. Pediatrics 1998;101:377-82.
22. Sil S, Kashikar-Zuck S. Understanding why cognitive-behavioral therapy is an effective treatment for adolescents with juvenile fibromyalgia. Int J Clin Rheumatol 2013;8:213-9.
23. Ablin J, Fitzcharles MA, Buskila D, Shir Y, Sommer C, Hauser W. Treatment of fibromyalgia syndrome: recommendations of recent evidence-based interdisciplinary guidelines with special emphasis on complementary and alternative therapies. Evid Based Complement Alternat Med 2013;2013:485272.
24. Moore RA, Derry S, Aldington D, Cole P, Wiffen PJ. Amitriptyline for neuropathic pain and fibromyalgia in adults. Cochrane Database Syst Rev 2012;12:CD008242.
25. Moore RA, Straube S, Wiffen PJ, Derry S, McQuay HJ. Pregabalin for acute and chronic pain in adults. Cochrane Database Syst Rev 2009;3: CD007076.
26. Uceyler N, Hauser W, Sommer C. A systematic review on the effectiveness of treatment with antidepressants in fibromyalgia syndrome. Arthritis Rheum 2008;59:1279-98.
27. Uceyler N, Sommer C, Walitt B, Hauser W. Anticonvulsants for fibromyalgia. Cochrane Database Syst Rev 2013;10:CD010782.

28. Sherry DD, Wallace CA, Kelley C, Kidder M, Sapp L. Short- and long-term outcomes of children with complex regional pain syndrome type I treated with exercise therapy. Clin J Pain 1999;15:218-23.
29. Brooke V, Janselewitz S. Outcomes of children with complex regional pain syndrome after intensive inpatient rehabilitation. PM R 2012;4:349-54.
30. Logan DE, Carpino EA, Chiang G, Condon M, Firn E, Gaughan VJ, et al. A day-hospital approach to treatment of pediatric complex regional pain syndrome: initial functional outcomes. Clin J Pain 2012;28:766-74.
31. Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Katz RS, Mease P, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. Arthritis Care Res 2010;62:600-10.
32. Gumming GR, Everatt D, Hastman L. Bruce treadmill test in children: normal values in a clinic population. Am J Cardiol 1978;41:69-75.
33. Bruininks RH, Bruininks BD. Bruininks-Oseretsky Test of Motor Proficiency, Second Edition. Minneapolis (MN): Pearson Assessment; 2005.
34. Kashikar-Zuck S, Flowers SR, Claar RL, Guite JW, Logan DE, Lynch-Jordan AM, et al. Clinical utility and validity of the Functional Disability Inventory among a multicenter sample of youth with chronic pain. Pain 2011;152:1600-7.
35. Kerns RD, Rosenberg R, Jamison RN, Caudill MA, Haythornthwaite J. Readiness to adopt a self-management approach to chronic pain: the Pain Stages of Change Questionnaire (PSOCQ). Pain 1997;72:227-34.
36. Price DD, McGrath PA, Rafii A, Buckingham B. The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. Pain 1983;17:45-56.
37. Varni JW, Seid M, Rode CA. The PedsQL: measurement model for the pediatric quality of life inventory. Med Care 1999;37:126-39.
38. Varni JW, Seid M, Kurtin PS. The PedsQL 4.0: reliability and validity of the Pediatric Quality of Life Inventory version 4.0 generic core scales in healthy and patient populations. Med Care 2001;39:800-12.
39. Varni JW, Seid M, Knight TS, Uzark K, Szer IS. The PedsQL 4.0 Generic Core Scales: sensitivity, responsiveness, and impact on clinical decision-making. J Behav Med 2002;25:175-93.
40. Varni JW, Burwinkle TM, Seid M, Skarr D. The PedsQL 4.0 as a pediatric population health measure: feasibility, reliability, and validity. Ambul Pediatr 2003;3:329-41.